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EDITORIAL

Are we ready to shorten the treatment duration for non-cavitary pulmonary tuberculosis?

SINCE THE EARLY 1980s, the American Thoracic Society has recommended that relapse rates for effective anti-tuberculosis treatment regimens not exceed 5%.[1] In this issue of the *Journal,* Phillips and colleagues counter that a 4-month regimen might be adequate for non-cavitary pulmonary tuberculosis (PTB) because the estimated relapse rate was 6.6%, only slightly higher than 5%, and because relapse was not associated with acquired bacillary resistance.[2] To advance the discussion, let us examine the rationale for recommending an overall relapse rate of ⩽5%, and whether it is appealing to shorten the current treatment duration for non-cavitary PTB.

The World Health Organization has recommended cure rates of ⩾85% and case detection rates of ⩾70% among new smear-positive cases as performance targets for global TB control.[3] The ultimate aim is the elimination of TB through a steady decline in its global prevalence and incidence by 5–10% annually. In endemic areas, a substantial proportion of TB patients are retreatment cases, comprising predominantly default or relapse cases. While the relapse rate of the standard rifamycin-based 6-month regimen is close to 1% for non-cavitary PTB, it exceeds 5% in the presence of cavitation and positive 2-month sputum culture, and is even higher when the initial treatment phase is intermittent.[4,5] An overall relapse rate of ⩽5%, together with high rates of case detection and cure, is thus probably necessary (although not sufficient) to eliminate TB.

It may be unattractive to shorten the current treatment of non-cavitary PTB if we take into consideration the following four factors. First, the relapse rate of non-cavitary PTB would increase by 5.4% rather than 1.6%, because the pooled relapse rate for the 6-month regimen is actually 1.2% and not 5%.[2] In endemic areas with high case densities, the cumulative effects of an estimated 5.4% increase in the relapse rate may substantially fuel TB transmission and ultimately increase the caseload.[6] Second, the actual relapse rate of a 4-month regimen for 'non-cavitary' PTB could exceed 6.6% because of the practical difficulty in reliably determining cavitation on chest radiograph in some patients.[7] Misclassification of cavitation is likely more common in a programme setting. Third, the higher relapse rate of a 4-month regimen may not always be offset by less treatment default. A study of TB treatment default in a programme setting showed that >60% of default among patients with bacteriologically confirmed PTB occurred within the first 2 months, and <20% after the first 4 months.[8] Finally, from the perspective of treatment supervision, when the same number of doses in the continuation phase of a 4-month daily regimen can be more efficaciously spaced out three times weekly in a 6-month regimen it may ease the labour-intensive task of supervision in settings with substantial TB burden.[4,9]

Clinical trials are underway to explore the effectiveness of new, shorter TB treatment regimens. Before this is possible, it may be more strategic to optimise the dosing schedule of, and adherence to, the current standard regimen, particularly in the first 2 months,[10] than to omit the last 2 months of standard treatment.

Kwok-Chiu Chang*
Timothy R. Sterling†
Wing-Wai Yew‡
*Tuberculosis and Chest Service
Department of Health
Hong Kong, China
†Vanderbilt University School of Medicine
Nashville, Tennessee, USA
‡Department of Microbiology
The Chinese University of Hong Kong
Hong Kong, China
e-mail: kc_chang@dh.gov.hk

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